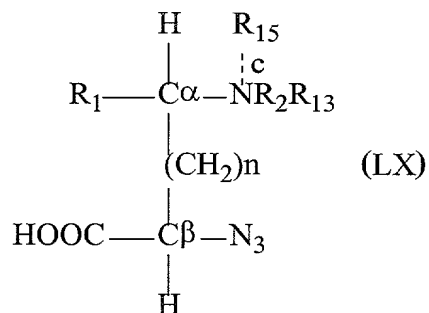


What is claimed is:

1. A non-natural amino acid compound having the formula LX:



wherein

n is an integer of from 1 to 4;

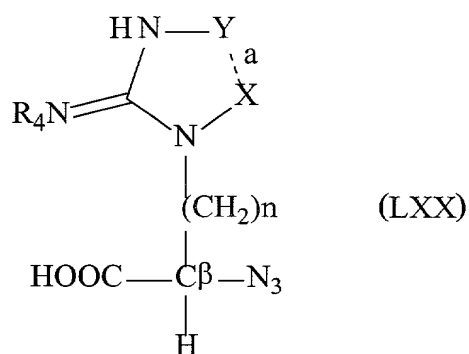
R₁, R₂, R₃, R₁₃, and R₁₅ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_α and C_β are carbon atoms and the stereochemistry at C_α and C_β is, independently, either R or S;

or the ester or salt thereof,

wherein when dashed line c is present, then R₁₅ is present, and when dashed line c is not present, then R₁₅ is not present; wherein when dashed line c is present, the compound is a salt comprising a counterion.

2. The compound of claim 1, wherein the stereochemistry at C_β is S.
3. The compound of claim 1, wherein R₁, R₂, and R₁₃ are, independently, hydrogen or methyl, and R₁₅ is methyl.
4. A non-natural amino acid compound of the formula LXX:



wherein

n is an integer of from 2 to 4;

when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

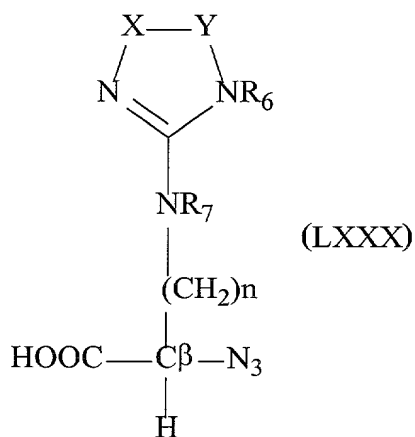
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R_4 is hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof.

5. A non-natural amino acid compound of the formula LXXX:



wherein

n is an integer of from 2 to 4;

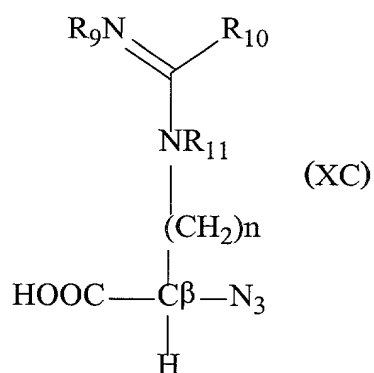
$X-Y$ is $(CH_2)_z$, wherein z is an integer of from 2 to 4;

R_6 and R_7 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof.

6. A non-natural amino acid compound of the formula XC:



wherein

n is an integer of from 2 to 4;

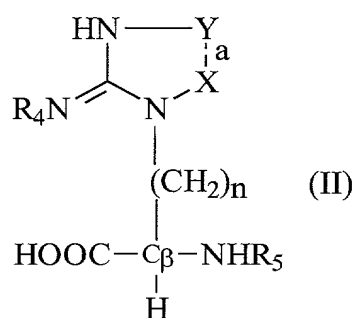
R_9 , R_{10} , and R_{11} are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;
or the ester or salt thereof.

7. A peptide comprising the non-natural amino acid of claim 1.

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8. A peptide comprising the non-natural amino acid of claim 4.
9. A peptide comprising the non-natural amino acid of claim 5.
10. A peptide comprising the non-natural amino acid of claim 6.
11. A method for screening a peptide containing a non-natural amino acid compound for an activity, comprising the steps of:
 - a) measuring a known activity or pharmacological activity of a peptide having a known amino acid sequence comprising at least one natural amino acid; and
 - b) measuring the same activity or pharmacological activity of a peptide having the same amino acid as in step (a), with the exception that at least one natural amino acid is substituted with a non-natural amino acid having the formula II, LX, LXX, LXXX, and/or XC:



wherein

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n is an integer of from 2 to 4;

when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

R₄ and R₅ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof, wherein

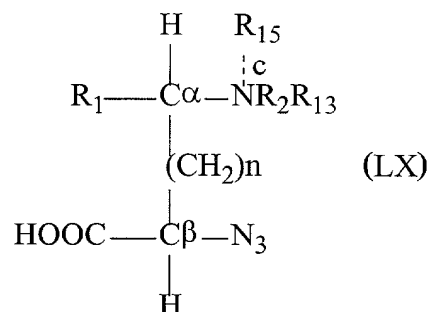
when n is 3, dashed line a is not present, R₄, X and Y are all hydrogen, and R₅ is methyl, then C_β is not S,

when n is 3, dashed line a is not present, X and R₅ are hydrogen, and Y and R₄ are methyl, then the stereochemistry at C_β is not R,

when dashed line a is not present, and R₄, R₅, X and Y are all hydrogen, then n is not 3,

when n is 4, dashed line a is not present, X and R₅ are hydrogen, and Y and R₄ are the same lower branched or straight chain alkyl, then C_β is not R, and

when n is 4, dashed line a is not present, and R₄, R₅, X and Y are all hydrogen, then the stereochemistry at C_β is not R;



wherein

n is an integer of from 1 to 4;

R₁, R₂, R₃, R₁₃, and R₁₅ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_α and C_β are carbon atoms and the stereochemistry at C_α and C_β is, independently, either R or S;

or the ester or salt thereof,

wherein when dashed line c is present, then R₁₅ is present, and when dashed line c is not present, then R₁₅ is not present; wherein when dashed line c is present, the compound is a salt comprising a counterion;



wherein

n is an integer of from 2 to 4;

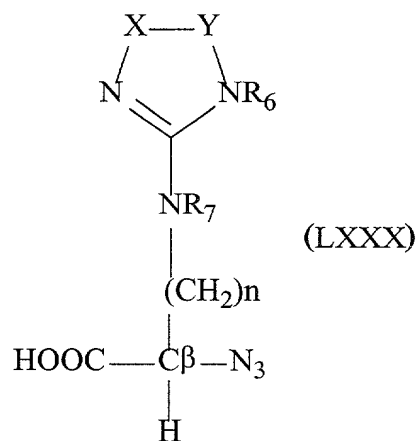
when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R₄ is hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;



wherein

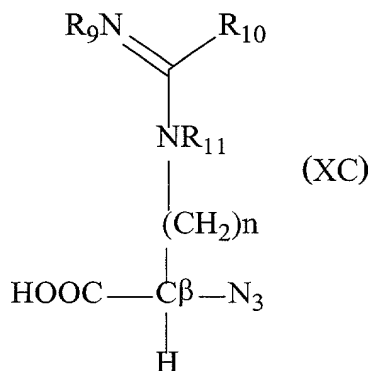
n is an integer of from 2 to 4;

X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R_6 and R_7 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of $\text{C}_1\text{-C}_5$; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof; or



wherein

n is an integer of from 2 to 4;

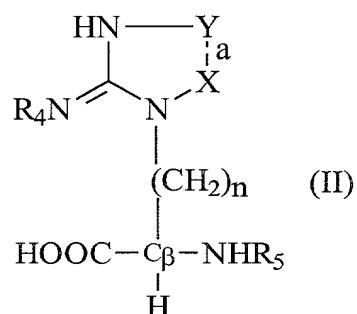
R₉, R₁₀, and R₁₁ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S; or the ester or salt thereof.

12. The method of claim 11, wherein the compound is substituted for the comparable at least one natural amino acid of lysine and/or arginine.
13. The method of claim 11, wherein the pharmacological activity is half-life, solubility, or stability.
14. The method of claim 11, wherein the pharmacological activity is body barrier passage.

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15. The method of claim 11, wherein the pharmacological activity is selectivity.
16. A method of treating or preventing in a subject a disease treated or prevented by the administration of a peptide containing a natural amino acid, comprising administering to the subject the known therapeutic peptide having, substituted for the natural amino acid, at least one non-natural amino acid having the formula II, LX, LXX, LXXX, and/or CX:



wherein

n is an integer of from 2 to 4;

when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

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R_4 and R_5 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof, wherein

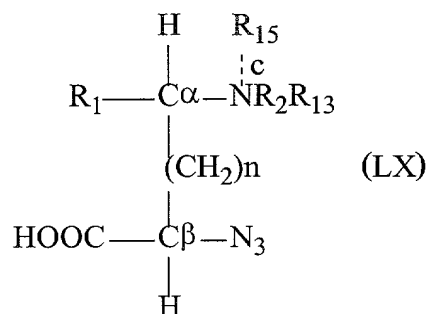
when n is 3, dashed line a is not present, R_4 , X and Y are all hydrogen, and R_5 is methyl, then C_β is not S,

when n is 3, dashed line a is not present, X and R_5 are hydrogen, and Y and R_4 are methyl, then the stereochemistry at C_β is not R,

when dashed line a is not present, and R_4 , R_5 , X and Y are all hydrogen, then n is not 3,

when n is 4, dashed line a is not present, X and R_5 are hydrogen, and Y and R_4 are the same lower branched or straight chain alkyl, then C_β is not R, and

when n is 4, dashed line a is not present, and R_4 , R_5 , X and Y are all hydrogen, then the stereochemistry at C_β is not R;



wherein

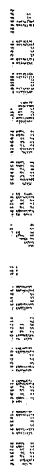
n is an integer of from 1 to 4;

R₁, R₂, R₃, R₁₃, and R₁₅ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_α and C_β are carbon atoms and the stereochemistry at C_α and C_β is, independently, either R or S;

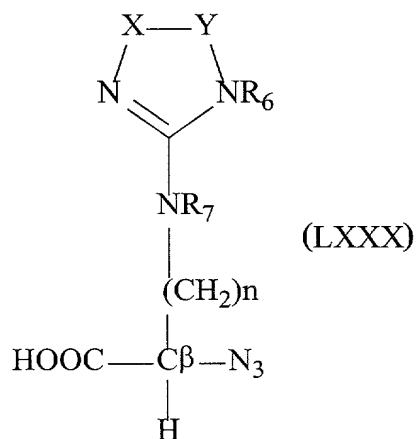
or the ester or salt thereof,

wherein when dashed line c is present, then R₁₅ is present, and when dashed line c is not present, then R₁₅ is not present; wherein when dashed line c is present, the compound is a salt comprising a counterion;

[illegible][illegible][illegible][illegible][illegible]

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[illegible]



wherein

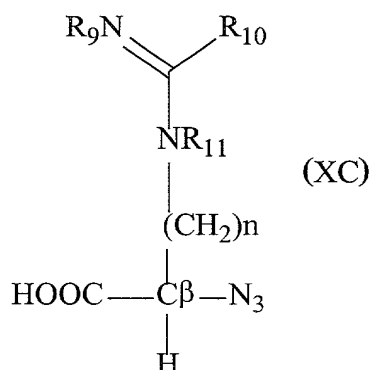
n is an integer of from 2 to 4;

X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R_6 and R_7 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of $\text{C}_1\text{-C}_5$; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof; or



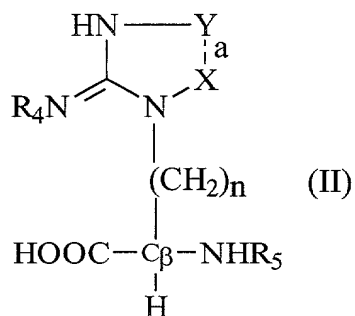
wherein

n is an integer of from 2 to 4;

R₉, R₁₀, and R₁₁ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S; or the ester or salt thereof.

17. The method of claim 16, wherein the natural amino acid is lysine and/or arginine.
18. A method of increasing the ability of a peptide to cross a body barrier of a subject, comprising substituting for at least one natural amino acid in the peptide at least one non-natural amino acid compound having the formula II, III, IV, LX, LXX, LXXX, and/or XC:



wherein

n is an integer of from 2 to 4;

when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

R₄ and R₅ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof, wherein

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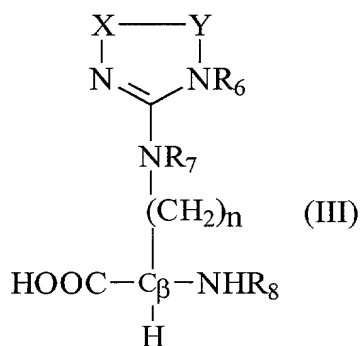
when n is 3, dashed line a is not present, R_4 , X and Y are all hydrogen, and R_5 is methyl, then C_β is not S,

when n is 3, dashed line a is not present, X and R_5 are hydrogen, and Y and R_4 are methyl, then the stereochemistry at C_β is not R,

when dashed line a is not present, and R_4 , R_5 , X and Y are all hydrogen, then n is not 3,

when n is 4, dashed line a is not present, X and R_5 are hydrogen, and Y and R_4 are the same lower branched or straight chain alkyl, then C_β is not R, and

when n is 4, dashed line a is not present, and R_4 , R_5 , X and Y are all hydrogen, then the stereochemistry at C_β is not R;



wherein

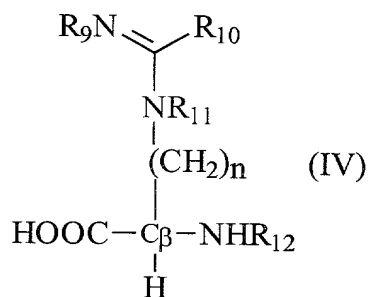
n is an integer of from 2 to 4;

X-Y is $(CH_2)_z$, wherein z is an integer of from 2 to 4;

R_6 , R_7 and R_8 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;

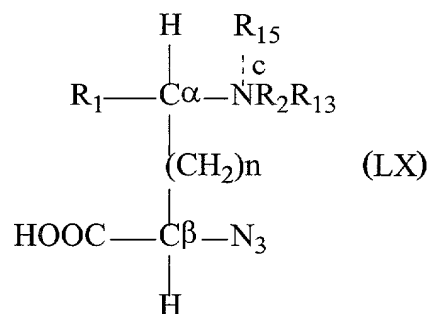


wherein

n is an integer of from 2 to 4;

R_9 , R_{10} , R_{11} and R_{12} are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;
or the ester or salt thereof;



wherein

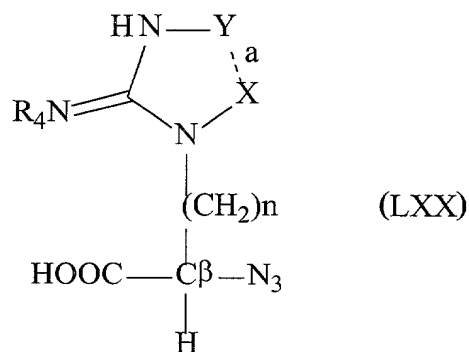
n is an integer of from 1 to 4;

R₁, R₂, R₃, R₁₃, and R₁₅ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_α and C_β are carbon atoms and the stereochemistry at C_α and C_β is, independently, either R or S;

or the ester or salt thereof,

wherein when dashed line c is present, then R₁₅ is present, and when dashed line c is not present, then R₁₅ is not present; wherein when dashed line c is present, the compound is a salt comprising a counterion;



wherein

n is an integer of from 2 to 4;

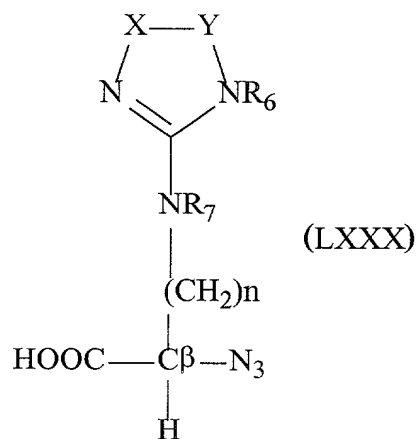
when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

R₄ is hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;



wherein

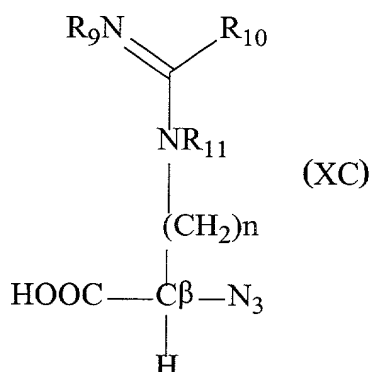
n is an integer of from 2 to 4;

X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R_6 and R_7 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of $\text{C}_1\text{-C}_5$; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof; or



wherein

n is an integer of from 2 to 4;

R₉, R₁₀, and R₁₁ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

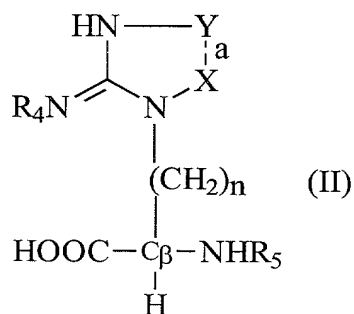
C_β is a carbon atom and the stereochemistry at C_β is either R or S; or the ester or salt thereof,

whereby the peptide having at least one non-natural amino acid is better able to cross the barrier than a peptide having no non-natural amino acid.

19. The method of claim 18, wherein the barrier comprises the blood brain barrier, a cell membrane, intestinal epithelium, skin, or blood-ocular.
20. The method of claim 18, wherein the barrier is the blood brain barrier.

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21. The method of claim 18, wherein the natural amino acid comprises arginine and/or lysine.
22. The method of claim 18, wherein the compound comprises:
- (a) a compound having the formula II, dashed line a is not present, n is 3, X, R₄, and R₅ are hydrogen, Y is methyl, and the stereochemistry at C_β is S;
 - (b) a compound having the formula II, dashed line a is not present, n is 3, X, R₄, and R₅ are hydrogen, Y is ethyl, and the stereochemistry at C_β is S;
 - (c) a compound having the formula II, dashed line a is present, n is 3, z is 2, R₄, and R₅ are hydrogen, and the stereochemistry at C_β is S; and
 - (d) a compound having the formula III, n is 3, X, R₆, R₇, and R₈ are hydrogen, and the stereochemistry at C_β is S.
23. A method of increasing the selectivity of a peptide, comprising substituting for at least one natural amino acid at least one non-natural amino acid having the formula II, III, IV, LX, LXX, LXXX, and/or XC:



wherein

n is an integer of from 2 to 4;

when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

R₄ and R₅ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof, wherein

when n is 3, dashed line a is not present, R₄, X and Y are all hydrogen, and R₅ is methyl, then C_β is not S,

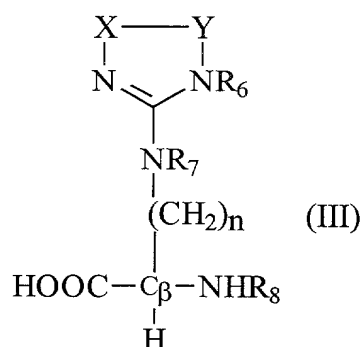
when n is 3, dashed line a is not present, X and R₅ are hydrogen, and Y and R₄ are methyl, then the stereochemistry at C_β is not R,

when dashed line a is not present, and R₄, R₅, X and Y are all hydrogen, then n is not 3,

when n is 4, dashed line a is not present, X and R₅ are hydrogen, and Y and R₄ are the same lower branched or straight chain alkyl, then C_β is not R, and

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when n is 4, dashed line a is not present, and R₄, R₅, X and Y are all hydrogen, then the stereochemistry at C_β is not R;



wherein

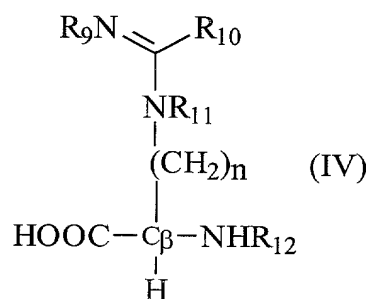
n is an integer of from 2 to 4;

X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

R₆, R₇ and R₈ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;

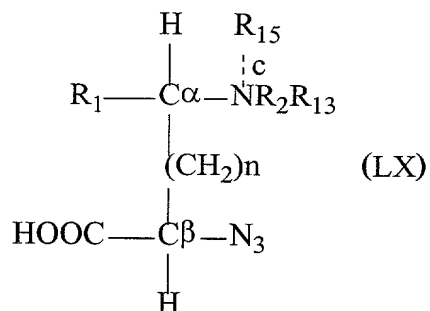


wherein

n is an integer of from 2 to 4;

R₉, R₁₀, R₁₁ and R₁₂ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S; or the ester or salt thereof;



wherein

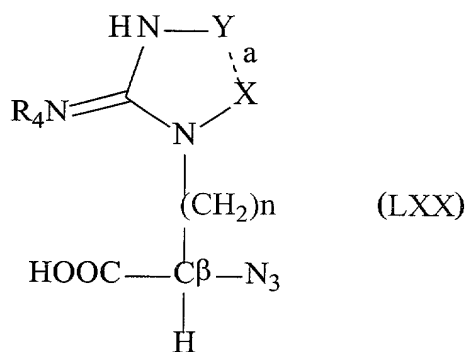
n is an integer of from 1 to 4;

R_1 , R_2 , R_3 , R_{13} , and R_{15} are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_α and C_β are carbon atoms and the stereochemistry at C_α and C_β is, independently, either R or S;

or the ester or salt thereof,

wherein when dashed line c is present, then R_{15} is present, and when dashed line c is not present, then R_{15} is not present; wherein when dashed line c is present, the compound is a salt comprising a counterion;



wherein

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n is an integer of from 2 to 4;

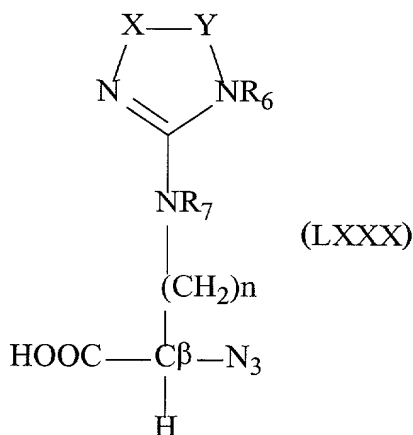
when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

R₄ is hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;



wherein

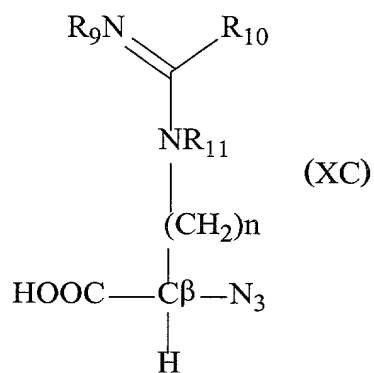
n is an integer of from 2 to 4;

X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R_6 and R_7 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of $\text{C}_1\text{-C}_5$; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof; or



wherein

n is an integer of from 2 to 4;

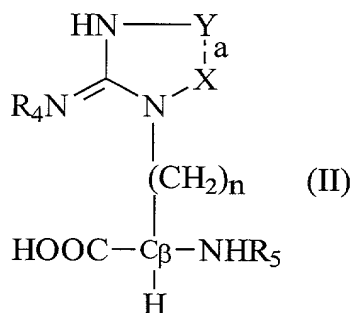
R_9 , R_{10} , and R_{11} are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of $\text{C}_1\text{-C}_5$; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof,

whereby the peptide having at least one non-natural amino acid is more selective than the peptide having no non-natural amino acid.

24. The method of claim 23, wherein the natural amino acid comprises arginine and/or lysine.
25. A method of increasing the resistance of a peptide to digestion by a peptidase, comprising substituting for at least one natural amino acid in the peptide at least one non-natural amino acid having the formula II, III, IV, LX, LXX, LXXX, and/or XC:



wherein

n is an integer of from 2 to 4;

when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

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when dashed line a is present, X-Y is $(CH_2)_z$, wherein z is an integer of from 2 to 4;

R_4 and R_5 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof, wherein

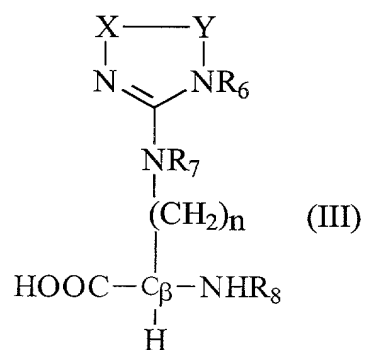
when n is 3, dashed line a is not present, R_4 , X and Y are all hydrogen, and R_5 is methyl, then C_β is not S,

when n is 3, dashed line a is not present, X and R_5 are hydrogen, and Y and R_4 are methyl, then the stereochemistry at C_β is not R,

when dashed line a is not present, and R_4 , R_5 , X and Y are all hydrogen, then n is not 3,

when n is 4, dashed line a is not present, X and R_5 are hydrogen, and Y and R_4 are the same lower branched or straight chain alkyl, then C_β is not R, and

when n is 4, dashed line a is not present, and R_4 , R_5 , X and Y are all hydrogen, then the stereochemistry at C_β is not R;



wherein

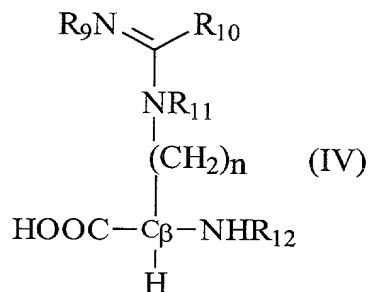
n is an integer of from 2 to 4;

X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R_6 , R_7 and R_8 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;

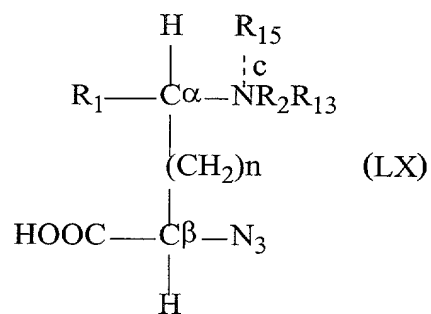


wherein

n is an integer of from 2 to 4;

R_9 , R_{10} , R_{11} and R_{12} are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;
or the ester or salt thereof;



wherein

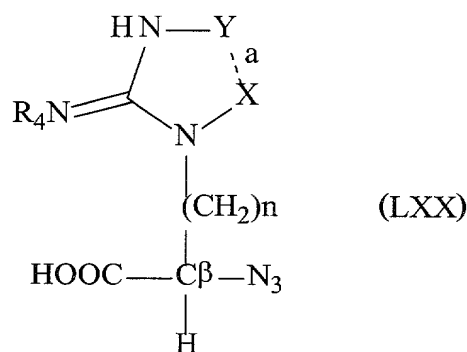
n is an integer of from 1 to 4;

R_1 , R_2 , R_3 , R_{13} , and R_{15} are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_α and C_β are carbon atoms and the stereochemistry at C_α and C_β is, independently, either R or S;

or the ester or salt thereof,

wherein when dashed line c is present, then R_{15} is present, and when dashed line c is not present, then R_{15} is not present; wherein when dashed line c is present, the compound is a salt comprising a counterion;



wherein

n is an integer of from 2 to 4;

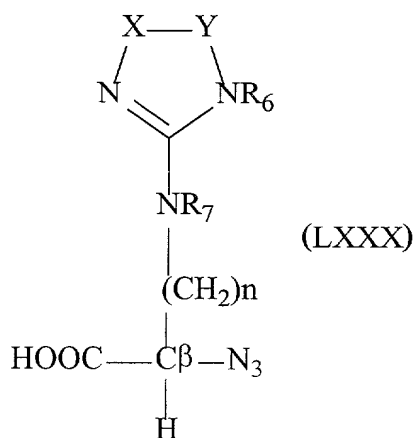
when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of $\text{C}_1\text{-C}_5$;

when dashed line a is present, X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R_4 is hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of $\text{C}_1\text{-C}_5$; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;



wherein

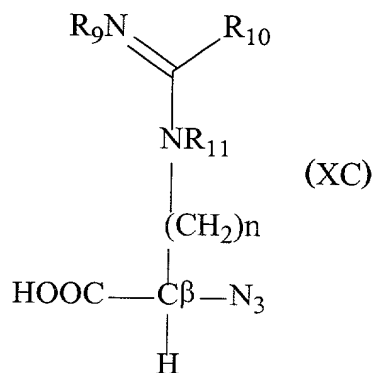
n is an integer of from 2 to 4;

X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R_6 and R_7 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of $\text{C}_1\text{-C}_5$; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof; or



wherein

n is an integer of from 2 to 4;

R₉, R₁₀, and R₁₁ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

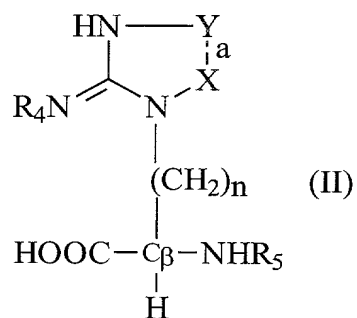
C_β is a carbon atom and the stereochemistry at C_β is either R or S; or the ester or salt thereof,

whereby the peptide having at least one non-natural amino acid is better able to resist digestion by a peptidase than a peptide having no non-natural amino acid.

26. The method of claim 25, wherein the natural amino acid comprises arginine and/or lysine.

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27. A method of treating or preventing in a subject a disease treated or prevented by the administration of a peptide that crosses a body barrier, comprising administering to the subject a peptide having, substituted for at least one natural amino acid at least one non-natural amino acid having the formula II, III, IV, LX, LXX, LXXX, and/or XC:



wherein

n is an integer of from 2 to 4;

when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

R₄ and R₅ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof, wherein

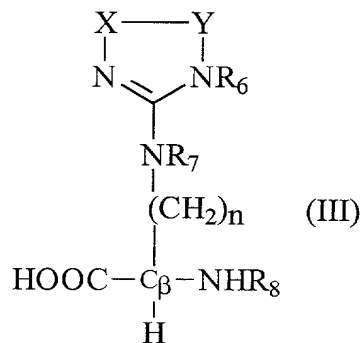
when n is 3, dashed line a is not present, R_4 , X and Y are all hydrogen, and R_5 is methyl, then C_β is not S,

when n is 3, dashed line a is not present, X and R_5 are hydrogen, and Y and R_4 are methyl, then the stereochemistry at C_β is not R,

when dashed line a is not present, and R_4 , R_5 , X and Y are all hydrogen, then n is not 3,

when n is 4, dashed line a is not present, X and R_5 are hydrogen, and Y and R_4 are the same lower branched or straight chain alkyl, then C_β is not R, and

when n is 4, dashed line a is not present, and R_4 , R_5 , X and Y are all hydrogen, then the stereochemistry at C_β is not R;



wherein

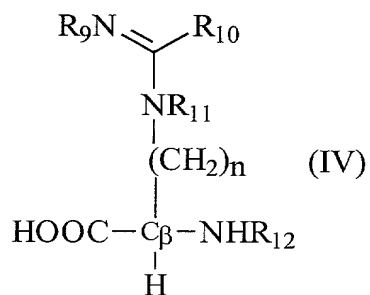
n is an integer of from 2 to 4;

X-Y is $(CH_2)_z$, wherein z is an integer of from 2 to 4;

R_6 , R_7 and R_8 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;



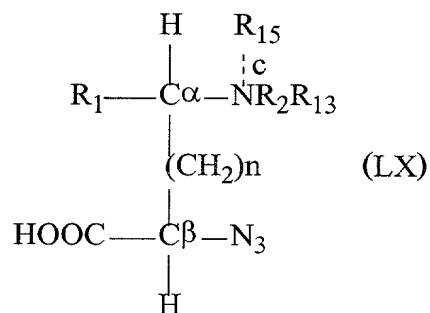
wherein

n is an integer of from 2 to 4;

R_9 , R_{10} , R_{11} and R_{12} are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

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C_β is a carbon atom and the stereochemistry at C_β is either R or S;
or the ester or salt thereof;



wherein

n is an integer of from 1 to 4;

R_1 , R_2 , R_3 , R_{13} , and R_{15} are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_α and C_β are carbon atoms and the stereochemistry at C_α and C_β is, independently, either R or S;

or the ester or salt thereof,

wherein when dashed line c is present, then R_{15} is present, and when dashed line c is not present, then R_{15} is not present; wherein when dashed line c is present, the compound is a salt comprising a counterion;



wherein

n is an integer of from 2 to 4;

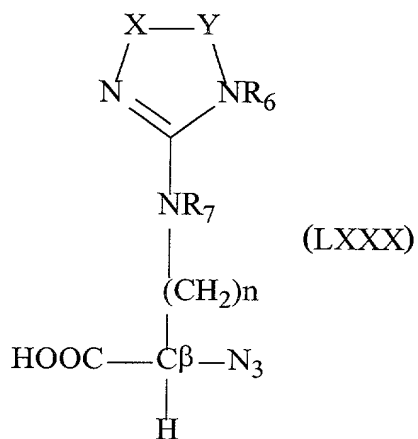
when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R₄ is hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;



wherein

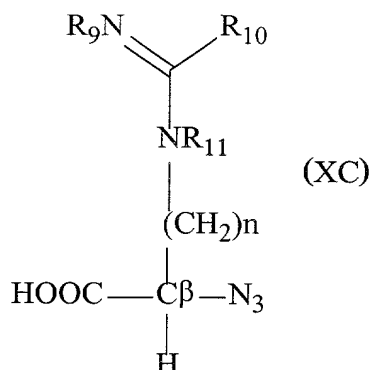
n is an integer of from 2 to 4;

X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R_6 and R_7 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of $\text{C}_1\text{-C}_5$; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof; or



wherein

n is an integer of from 2 to 4;

R₉, R₁₀, and R₁₁ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

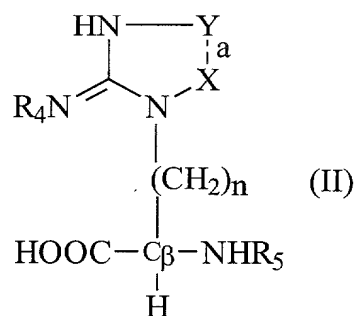
C_β is a carbon atom and the stereochemistry at C_β is either R or S; or the ester or salt thereof,

whereby the peptide having at least one non-natural amino acid crosses the body barrier in higher amounts than the peptide having no non-natural amino acid.

28. A method of treating or preventing in a subject a disease of the brain treated or prevented by the administration of a peptide containing a natural amino acid, comprising administering to the subject the known therapeutic peptide having, substituted for the natural amino acid, at least one non-

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natural amino acid having the formula II, III, IV, LX, LXX, LXXX, and/or XC:



wherein

n is an integer of from 2 to 4;

when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

R₄ and R₅ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof, wherein

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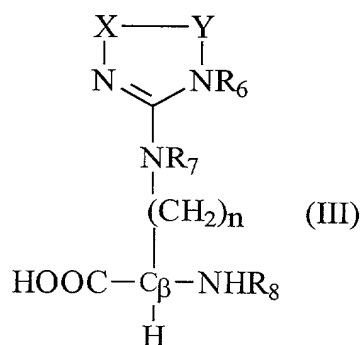
when n is 3, dashed line a is not present, R₄, X and Y are all hydrogen, and R₅ is methyl, then C_β is not S,

when n is 3, dashed line a is not present, X and R₅ are hydrogen, and Y and R₄ are methyl, then the stereochemistry at C_β is not R,

when dashed line a is not present, and R₄, R₅, X and Y are all hydrogen, then n is not 3,

when n is 4, dashed line a is not present, X and R₅ are hydrogen, and Y and R₄ are the same lower branched or straight chain alkyl, then C_β is not R, and

when n is 4, dashed line a is not present, and R₄, R₅, X and Y are all hydrogen, then the stereochemistry at C_β is not R;



wherein

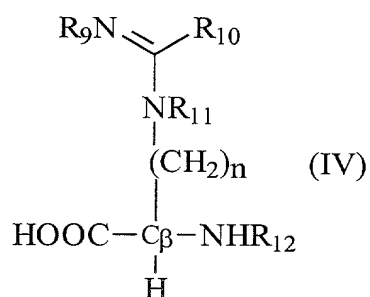
n is an integer of from 2 to 4;

X-Y is $(CH_2)_z$, wherein z is an integer of from 2 to 4;

R_6 , R_7 and R_8 are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;

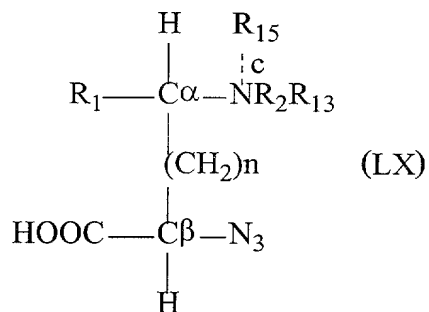


wherein

n is an integer of from 2 to 4;

R_9 , R_{10} , R_{11} and R_{12} are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C_1 - C_5 ; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;
or the ester or salt thereof;



wherein

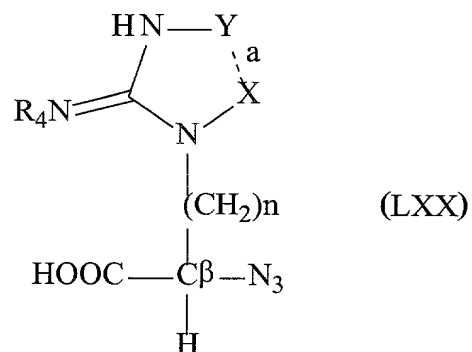
n is an integer of from 1 to 4;

R₁, R₂, R₃, R₁₃, and R₁₅ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_α and C_β are carbon atoms and the stereochemistry at C_α and C_β is, independently, either R or S;

or the ester or salt thereof,

wherein when dashed line c is present, then R₁₅ is present, and when dashed line c is not present, then R₁₅ is not present; wherein when dashed line c is present, the compound is a salt comprising a counterion;



wherein

n is an integer of from 2 to 4;

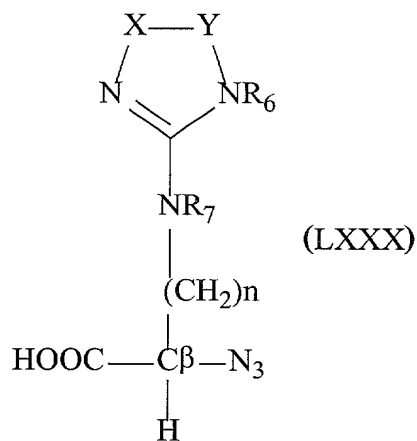
when dashed line a is not present, X and Y are independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅;

when dashed line a is present, X-Y is (CH₂)_z, wherein z is an integer of from 2 to 4;

R₄ is hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof;



wherein

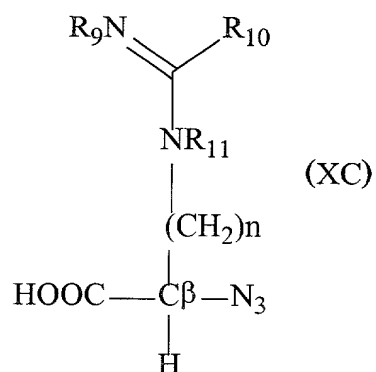
n is an integer of from 2 to 4;

X-Y is $(\text{CH}_2)_z$, wherein z is an integer of from 2 to 4;

R₆ and R₇ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S;

or the ester or salt thereof; or



wherein

n is an integer of from 2 to 4;

R₉, R₁₀, and R₁₁ are, independently, hydrogen or lower branched or straight chain alkyl, alkenyl or alkynyl of C₁-C₅; and

C_β is a carbon atom and the stereochemistry at C_β is either R or S; or the ester or salt thereof.